REMARKS

Reconsideration and allowance of the subject application are respectfully requested.

Claims 9, 25 and 31-52 are pending in the application.

Claim 49 has been amended to be dependent upon claim 44. No new matter has been added. Claim 49 has not been amended to overcome prior art.

Claim 37 has been amended to replace "comprising" with "consisting essentially of". Claims 37 and 38 have been amended to remove reference to the active substance. Claims 37 and 38 have been amended to recite that the matrix material-containing compound is directly compressible into larger units or tablets without requiring binders. Basis for this statement can be found in the originally filed application including in examples 3 and 4, in which only 0.5% Aerosil and 1% magnesium stearate were added to the spray-dried compound and direct compression was performed without the use of binders. Furthermore, the language "directly compressible" means that no binders are required in that the compound can be directly compressed. The use of binders would be indirect compression. No new matter has been added.

Basis for new claims 50-52 can be found in the originally filed application, including at page 23 of the official translation in lines 3-4 and line 14. Example describes the preparation of a compound containing acetylsalicylic acid, in which the drug was dispersed in water. Further basis for new claims 51 and 52 can be found at pending claims 37 and 38 respectively. No new matter has been added.

The rejection of claims 31-33, 37-49, 9 and 25 under 35 U.S.C. § 102 over Chen is respectfully traversed. The claimed invention is not anticipated by Chen for the many reasons of record and for the following reasons.

Chen describes the dissolution of one specific drug (sodium diclofenac) in water, an excipient is added (e..g. lactose), a non-soluble polymer is dispersed (one specific

Eudragit type) and the powder is spray-dried. However, this is only part of what Chen teaches. Chen continues by saying that the spray dried product needs to be further processed to a tablet, requiring the addition of a mixture of microcristalline cellulose and starch to bind it together. See column 3, lines 11-26 of Chen. The mixture of Chen does not bind without an additional excipient and, thus, has a different structure than the claimed invention.

In contrast to Chen, the claimed invention is directly compressible into a tablet and no further binders are required. Chen discloses the opposite of the claimed invention, indirect compression using binders. For this reason alone, Chen cannot anticipate the claimed invention.

New claims 50 to 52 require that the use of an active agent suspended in the compound. Chen does not disclose an active agent suspended in the compound.

For these reasons and the reasons of record, the claimed invention cannot be anticipated by Chen. Accordingly, withdrawal of the Section 102 rejection is respectfully requested.

The rejection of claims 37-49, 9, 25, 31, and 35-36 under 35 U.S.C. § 102 over Norling is respectfully traversed. The claimed invention is not anticipated by Norling for the following reasons.

The matrix material in the claimed invention is organic. Claim 37 recites that the matrix material comprises a cellulose derivative, and claims 38 and 44 recites that the matrix material comprises at least one polymer or lipid. In contrast, Norling teaches an inorganic matrix material. For this reason alone, the Section 102 rejection should be withdrawn.

The Examiner argues on page 6, lines 3-7 of the Office Action that Norling teaches using organic compounds. However, Norling discloses that these compounds are <u>not the core forming material</u>. The organic compounds disclosed in Norling are drugs to load the particles and are used in addition to calcium carbonate (example 2 and 3) or are used to coat the cores (example 4). Example 5 only describes the filling of capsules with products from example 3 and 4.

The consisting essentially language of claim 37 and 38 exclude the use of the salts

disclosed in Norling as an essential ingredient. The salts in Norling are clearly an essential ingredient and are provided in a large amount, upwards of 80%. For this reason alone the Section 102 rejection should be withdrawn.

According to the Examiner on page 6 of the Office Action, if a prior art structure is capable of performing the intended use, then it meets the claim. This simply is not true. Norling must cite the structure of the claimed invention in structure claims 9, 25 and 31-38 or the method of claims 44-49 in order to anticipate the claimed invention. There are no intended use claims recited.

According to the Examiner's logic, for example, when a zero order release from a therapeutic delivery system "osmogit" oral release system (osmotic pump) is perfomed, and it is described to have also zero release from a multiparticulate tablet which releases after fast disintegration pellets (Beloc ZOK product Applicant referred to in the previous correspondence), then the second system would not have been patentable anymore. That means after publishing the first time a zero order release system, no system showing also zero order release would have been patentable. In contrast, patent law is very clear that a system is patentable when it performs the same release but has different features in structure (e.g. pump versus pellet) that distinguish the two inventions. The same is valid when comparing the present invention with Norling.

Both the claimed invention and Norling show prolonged release. Norling achieves prolonged release via coated pellets after desintegration of the tablet, which acts only as unit to hold the pellets together, reasons of convenient administration to the patient. In contrast, the present invention has a very different structure, i.e. the compressed tablet remains intact and prolonged release is achieved by a different principle, matrix diffusion according to Higuchi law, not according to Law by Fick.

The very different structures between the claimed invention and Norling has been demonstrated by the drawings provided in Applicant's Response filed on November 13, 2002.

As stated previously, the Higuchi and the Fick law describe release from different structures. The Higuchi law cannot be applied when no matrix structure is there. That

means the physical laws applicable prove that there are different structures. This is physics and cannot be denied.

On top of this, there is no intended use claimed, what is claimed is a structure and process of achieving it.

In the claimed invention, the excipient phase of the formulation is coherent, such that when it is directly compressed into a tablet is very different in structure to coated cores.

Contrary to the Examiner argument on page 7, lines 1-3 of the Office Action, Norling cannot meet the physical limitations of the instant claims because the Noreling structure of a coated core is very different from the directly compressible powder of the claimed invention. As stated above, Norling teaches that the matrix material is only inorganic, salts, (all organic compounds used by Norling are drugs, not matrix material). In contrast, the matrix materials in the present invention are organic.

On page 7, lines 4-7 of the Office Action, the Examiner did not accept the German encyclopedia because no translation was provided. Therefore, Applicant now refers to: Encyclopedia of Pharmaceutical Technology, J. Swarbrick, J.C. Boylan (eds.), Marcel Dekker, New York, 2002, Vol. 3, page 2067, which describes pellets as a special pharmaceutical formulation that is clearly defined. On 2068-2078, the production methods are described which are various methods but no spray drying. From this teaching, there is a clear difference between pellet and compound.

Applicant submits that the Rule 132 Declaration does not merely provide "anecdotal arguments" as alleged by the Examiner, but rather provides experimental evidence and scientific reasoning demonstrating the patentable differences between the claimed invention and the cited prior art.

In view of the many differences between the claimed invention and Norling, the Section 102 rejection should be withdrawn.

The rejection of claims 1, 2, 9, 13, 15, 16, 19-26 and 31-35 under 35 U.S.C. § 103 over Chen in view of Norling is respectfully traversed. The claimed invention is not taught or

suggested by the theoretical combination of Chen and Norling for the many reasons of record, the many reasons provided herein above, and for the following reasons.

One of ordinary skill in the art would not be motivated to combine Norling with Chen. Norling teaches an inorganic core that is coated to provide prolonged release. Chen teaches coated microcapsules that are bound together with neocel and flo-starch to form tablets (column 3, lines 20-26 of Chen). There is no motivation provided in either reference to replace the inorganic core of Norling with the coated microcapsules of Chen that are bound together with starch. The references teach very different methods and structures. Chen binds the matrix with inorganic salts. Norling binds the spray-dried particles with starch and neocel. For this reason alone, the Section 103 rejection should be withdrawn.

Even if Chen and Norling were combined, the theoretical combination of references would not teach or suggest the claimed invention for the following reasons.

All of the present claims require that the particles have a structure such that they are directly compressible into tablets to provide prolonged release. Directly compressible means without the use of additional binders such as starch and neocel. In contrast, the combination of Chen and Norling teaches (1) to use the coated spray dried particles that are bound together using neocel and starch of Chen in a coated tablet of Norling to provide prolonged release, or (2) to use the inorganic matrix material of Norling in the particles of Chen and then add neocel and flo-starch to form a tablet. No combination of Chen and Norling provides a compound having a structure such that it is directly compressible into a tablet (without the use of neocel and flo-starch according to Chen or inorganic salts according to Norling) to provide prolonged release properties (without the use of a coating as taught by both Norling and Chen). Thus, Chen and Norling both teach away from the claimed invention because they teach to use a coating to provide prolonged release and to use different structures to form the tablets.

The unexpected advantages of being able to provide prolonged release properties without the use of the coatings taught by both Norling and Chen and to provide tablets without the use of inorganic salts (Norling) or neocel and starch (Chen), demonstrates that

the claimed invention is not obvious from this combination of references. For this reason alone the Section 103 rejection should be withdrawn.

The Examiner argues on pages 7-8 of the Office Action that one of ordinary skill in the art would have made modifications in the spray-drying process of Chen to improve flowability via changes in the particle size. It is text book knowledge that the fowability of powders changes with size. Especially fine powders as produced by Chen are poorly flowable. From this, of course one can assume that Chen also did these modifications since most scientists do when spray drying. From reading and understanding Chen, one skilled in the art would conclude that Chen did not succeed because there is nothing disclosed about such particle size in his patent. Such a lack of a teaching in a patent leads to the conclusion that it did not work. Furthermore, the discussion about this is moot, because the present claims recite a structure and method that is very different from the theoretical structures disclosed in Chen and Norling.

The claimed particle sizes in Norling and present claim 36 are not the same for the following reasons:

> Norling discloses that 50% of the cores before coating should have a size between 90-225 µm (column 4, line 60).
>
> Present claim 36 recites size distributions: 100% between 1µm and 630 µm, 50-80% between 63 µm and 400 µm. These are sizes of the final product.
>
> That means there is no size specification by Norling of the final product (i.e. the coated cores), from this no optimum size for flowability can be derived from Norling because he processes the cores (size specified) to coated cores. The size after coating is not specified. Norling only specifies the size of his starting material.

In view of the many differences between the claimed invention and the theoretical combination of Chen and Norling and the unexpected advantages of the claimed invention, withdrawal of the subject application is respectfully requested.

In response to the Examiner's objection to the Information Disclosure Statement filed November 13, 2002, the filed herewith Request for Continued Examination requests full consideration of that Information Disclosure Statement. Thus, instead of charging the fee set forth in 37 CFR 1.17(p), please fully consider that Information Disclosure Statement in accordance with 37 CFR 1.114.

In view of all of the objections and rejections of record having been addressed, it is believed that the present application is in condition for allowance and Notice to that effect is respectfully requested.

Respectfully submitted,

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